Sterne Kessler Goldstein Fox
ATTORNEYS AT LAW

Robert Greene Sterne
Edward J. Kessler
Jorge A. Goldstein
David K.S. Cornwell
Robert W. Esmond
Tracy-Gene G. Durkin
Michele A. Cimbala
Michael B. Ray
Robert E. Sokohl
Eric K. Steffe
Michael Q. Lee
Steven R. Ludwig
John M. Covert
Linda E. Alcorn
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Lawrence B. Bugaisky
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Rodney G. Maze
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Michael A. Specht*
Andrea J. Kamage
Tracy L. Muller*

Jon E. Wright*
LuAnne M. Yuricek*

Registered Patent Agents•
Karen R. Markowicz
Nancy J. Leith
Ann E. Summerfield
Helene C. Carlson
Gaby L. Longsworth
Matthew J. Dowd
Aaron L. Schwartz
Angelique G. Uy
Boris A. Matvenko
Mary B. Tung
Katrina Y. Pei
Bryan L. Skelton
Robert A. Schwartzman
John J. Figueroa

Timothy A. Doyle
Jennifer R. Mahalingappa
Teresa A. Colella
Jeffrey S. Lundgren
Victoria S. Rutherford
W. Brian Edge

Senior Counsel
Samuel L. Fox
Kenneth C. Bass III
Lisa A. Dunner

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February 14, 2003

WRITER'S DIRECT NUMBER:
(202) 772-8673
INTERNET ADDRESS:
JCOVERT@SKGF.COM

Via Facsimile

Commissioner for Patents
Washington, D.C. 20231

Confirmation Copy Via Hand Carry
Group Art Unit 1626
Examiner G. Shameem

Re: U.S. Utility Patent Application
Appl. No. 09/814,123; Filed: March 22, 2001
For: **Aryl Substituted Pyrazoles, Triazoles and Tetrazoles, and the Use Thereof**
Inventors: HOGENKAMP *et al.*
Our Ref: 1861.1270001/JMC/THN

Sir:

Transmitted herewith for appropriate action are the following documents:

1. Supplemental Amendment and Reply; and

2. One (1) return postcard.

It is respectfully requested that the attached postcard be stamped with the date of filing of these documents, and that it be returned to our courier. In the event that extensions of time are necessary to prevent abandonment of this patent application, then such extensions of time are hereby petitioned.

The U.S. Patent and Trademark Office is hereby authorized to charge any fee deficiency, or credit any overpayment, to our Deposit Account No. 19-0036.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.

John M. Covert
Attorney for Applicants
Registration No. 38,759

Enclosures

SKGF_DC1:102710.1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

HOGENKAMP *et al.*

Appl. No. 09/814,123

Filed: March 22, 2001

For: **Aryl Substituted Pyrazoles, Triazoles and Tetrazoles, and the Use Thereof**

Confirmation No. 2060

Art Unit: 1626

Examiner: Shameem, G.

Atty. Docket: 1861.1270001/JMC/THN

Supplemental Amendment and Reply

Commissioner for Patents
Washington, D.C. 20231

Sir:

In reply to the Examiner's request during a telephone conference of February 4, 2003, Applicants submit the following Amendment and Remarks. This Amendment is provided in the following format:

(A) A clean version of each replacement paragraph/section/claim along with clear instructions for entry;

(B) Starting on a separate page, appropriate remarks and arguments. 37 C.F.R. § 1.111 and MPEP 714; and

(C) Starting on a separate page, a marked-up version entitled: "Version with markings to show changes made."

It is not believed that extensions of time or fees for net addition of claims are required beyond those that may otherwise be provided for in documents accompanying this paper. However, if additional extensions of time are necessary to prevent abandonment of this application, then such extensions of time are hereby petitioned under 37 C.F.R. § 1.136(a), and any fees required therefor (including fees

for net addition of claims) are hereby authorized to be charged to our Deposit Account No. 19-0036.

Amendment

In the Claims:

Please substitute the following claim 3 for the pending claim 3:

3. (Once Amended) A compound of claim 2, wherein R_{10} is selected from the group consisting of C_{1-6} alkyl, C_{2-6} alkenyl, OR_{10}, amino, C_{1-6} alkylamino, di(C_{1-6})alkylamino, C_{2-6} alkenylamino, and di(C_{1-6})alkylamino(C_{2-6})alkenyl.

Please substitute the following claim 15 for the pending claim 15:

15. (Three Times Amended) A compound of claim 1, wherein:

R_1 is $C(O)R_{10}$, $CH_2C(O)R_{10}$, or SO_2R_{10};

X is O or S;

R_{10} is amino, optionally substituted C_1-C_6 alkyl, or a heterocycle;

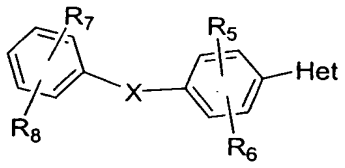
R_2, and R_3 are independently hydrogen, C_1-C_6 alkyl, C_1-C_6 alkylthio or C_1-C_6 alkylsulfinyl,

R_5 and R_6 are as defined in claim 1, and

R_7 and R_8 are independently selected from the group consisting of hydrogen, halo, halo(C_1-C_6)alkyl, C_1-C_6 alkyl, hydroxy(C_1-C_6)alkyl, amino(C_1-C_6)alkyl, carboxy(C_1-C_6)alkyl, alkoxy(C_1-C_6)alkyl, nitro, amino, C_1-C_6 acylamino, amide, hydroxy, thiol, C_1-C_6 acyloxy, C_1-C_6 alkoxy, carboxy, carbonylamido and C_1-C_6 alkylthiol.

Please substitute the following claim 16 for the pending claim 16:

16. (Three Times Amended) A compound of Formula *I*:



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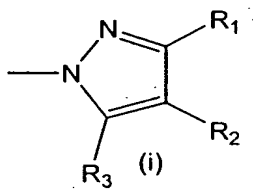
or a pharmaceutically acceptable salt, prodrug or solvate thereof, wherein

X is O or S;

Het is



R_1 is $C(O)R_{10}$, $CH_2C(O)R_{10}$, or SO_2R_{10} wherein R_{10} is amino, all of which are optionally substituted;

R_2 and R_3 are independently hydrogen, C_1-C_6 alkyl, C_1-C_6 alkylthio or C_1-C_6 alkylsulfinyl; and

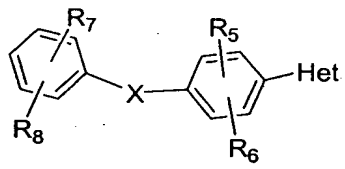
R_5, R_6, R_7 and R_8 are independently selected from the group consisting of hydrogen, halo, halo(C_1-C_6)alkyl, C_1-C_6 alkyl, hydroxy(C_1-C_6)alkyl, amino(C_1-C_6)alkyl, carboxy(C_1-C_6)alkyl, alkoxy(C_1-C_6)alkyl, nitro, amino, C_1-C_6 acylamino, amide, hydroxy, thiol, C_1-C_6 acyloxy, C_1-C_6 alkoxy, carboxy, carbonylamido and C_1-C_6 alkylthiol.

Please substitute the following claim 17 for the pending claim 17:

17. (Once Amended) A pharmaceutical composition, comprising the compound of any one of claims 1, 16, 22, or 25 and a pharmaceutically acceptable carrier.

Please substitute the following claim 22 for the pending claim 22:

22. (Three Times Amended) A compound of Formula *I*:



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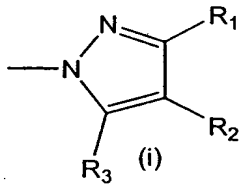
or a pharmaceutically acceptable salt, prodrug or solvate thereof, wherein

X is O or S;

Het is



(i)

R_1 is $C(O)R_{10}$, wherein R_{10} is amino, all of which are optionally substituted;

R_2 and R_3 are independently hydrogen, C_1-C_6 alkyl, C_1-C_6 alkylthio or C_1-C_6 alkylsulfinyl; and

R_5, R_6, R_7 and R_8 are independently selected from the group consisting of hydrogen, halo, halo(C_1-C_6)alkyl, C_1-C_6 alkyl, hydroxy(C_1-C_6)alkyl, amino(C_1-C_6)alkyl, carboxy(C_1-C_6)alkyl, alkoxy(C_1-C_6)alkyl, nitro, amino, C_1-C_6 acylamino, amide, hydroxy, thiol, C_1-C_6 acyloxy, C_1-C_6 alkoxy, carboxy, carbonylamido and C_1-C_6 alkylthiol.

Please add the following new claims 28-31:

28. (New) A method of treating a disorder responsive to the blockade of sodium channels in a mammal suffering therefrom, comprising administering to a mammal in need of such treatment an effective amount of the compound as claimed in any one of claims 1, 16, 22, or 25.

29. (New) A method for treating or ameliorating neuronal loss following global and focal ischemia; treating or ameliorating neurodegenerative conditions; treating or ameliorating pain or tinnitus; treating or ameliorating manic depression; providing local anesthesia; treating arrhythmias, or treating convulsions, comprising administering to a mammal in need of such treatment an effective amount of the compound as claimed in any one of claims 1, 16, 22, or 25.

30. (New) The method of claim 29, wherein the method is for treating or ameliorating pain and said pain is one of neuropathic pain, surgical pain or chronic pain.

31. (New A method of alleviating seizure activity in an animal subject, comprising administering to a mammal in need of such treatment an effective amount of a compound of any one of claims 1, 16, 22, or 25.

Remarks

Reconsideration of this Application is respectfully requested.

The Examiner requested on February 4, 2003, that claims 3, 15, 16, and 22 be amended by canceling the reference to "N-morpholinyl", "N-pyrrolidinyl", and "N-piperazinyl" as definitions for R_{10}, and that copies of the references listed on Form PTO-1449 resubmitted on May 9, 2002, be resubmitted.

During a telephone conference on February 5, 2003, the Examiner agreed that claim 15 can be amended by canceling the phrase "selected from the group consisting of N-morpholinyl, N-pyrrolidinyl, and N-piperazinyl" from the definitions of R_{10}, leaving the term "heterocycle" as a definition for R_{10}.

During a telephone conference of February 13, 2003, it was brought to the Examiner's attention that Applicants wish to amend claim 17, directed to pharmaceutical compositions, to be dependent also on independent claims 22 and 25 in addtion to claims 1 and 16. Furthermore, the Examiner indicated that he is willing to rejoin and consider the method claims 18-21, canceled in the previous Amendment of November 27, 2002, as long as they are specifically adapted to the allowable compounds and they are amended is such as way that no § 112, paragraph issues rise. Specifically, the Examiner requested the deletion of the term "preventing" from all the method claims.

Applicants resubmitted the references originally submitted along with Form PTO-1449 accompanying Applicants' Information Disclosure Statement, filed December 13, 2001 and resubmitted by facsimile on May 9, 2002, on February 13,

2003 via hand carry. Applicants respectfully request the Examiner to provide a copy of the initialed and signed PTO-1449 forms.

Claims 3, 15, 16, 17, and 22 are sought to be amended, and new claims 28-31 are sought to be added. Claims 3, 15, 16, and 22 have been amended by amending the definitions for R_{10} as requested by the Examiner. Applicants submit that no new matter has been introduced by this amendment since deletion of individual members of a Markush expression does not constitute new matter. *See In re Johnson and Farnham*, 558 F.2d 1008, 1019, 194 U.S.P.Q. 187, 196 (CCPA 1977). Claim 17 has been amended by amending the dependencies. Specifically, claim 17 has been amended to be dependent on all independent compound claims 1, 16, 22, and 25. Support for this amendment can be found in the original specification and claims as filed.

New claims 28-31 find support in the original claims 18-21. New claims 28-31 are specifically adapted to the allowable compounds. Further, none of claims 28-31 include the term "preventing."

These changes are believed to introduce no new matter, and their entry is respectfully requested. Upon entry of the foregoing amendment, claims 1-10, 15-17 and 22-31 are pending in the application, with claims 1, 16, 22 and 25 being the independent claims.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding issues raised by the Examiner and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Supplemental Amendment and Reply is respectfully requested.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.

John M. Covert

John M. Covert
Attorney for Applicants
Registration No. 38,759

Date: Feb. 14, 2003

1100 New York Avenue, N.W.
Suite 600
Washington, D.C. 20005-3934
(202) 371-2600

Version with markings to show changes made

New claims 28-31 have been added.

Claims 3, 15, 16, 17, and 22 have been amended as follows:

3. (Once Amended) A compound of claim 2, wherein R_{10} is selected from the group consisting of C_{1-6} alkyl, C_{2-6} alkenyl, OR_{10}, amino, C_{1-6} alkylamino, di(C_{1-6})alkylamino, C_{2-6} alkenylamino, and di(C_{1-6})alkylamino(C_{2-6})alkenyl[, N-morpholinyl, N-pyrrolidinyl, and N-piperazinyl].

15. (Three Times Amended) A compound of claim 1, wherein:

R_1 is $C(O)R_{10}$, $CH_2C(O)R_{10}$, or SO_2R_{10};

X is O or S;

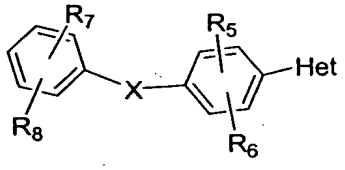
R_{10} is amino, optionally substituted C_1-C_6 alkyl, or a heterocycle [selected from the group consisting of N-morpholinyl, N-pyrrolidinyl and N-piperazinyl];

R_2, and R_3 are independently hydrogen, C_1-C_6 alkyl, C_1-C_6 alkylthio or C_1-C_6 alkylsulfinyl,

R_5 and R_6 are as defined in claim 1, and

R_7 and R_8 are independently selected from the group consisting of hydrogen, halo, halo(C_1-C_6)alkyl, C_1-C_6 alkyl, hydroxy(C_1-C_6)alkyl, amino(C_1-C_6)alkyl, carboxy(C_1-C_6)alkyl, alkoxy(C_1-C_6)alkyl, nitro, amino, C_1-C_6 acylamino, amide, hydroxy, thiol, C_1-C_6 acyloxy, C_1-C_6 alkoxy, carboxy, carbonylamido and C_1-C_6 alkylthiol.

16. (Three Times Amended) A compound of Formula *I*:



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or a pharmaceutically acceptable salt, prodrug or solvate thereof, wherein

X is O or S;

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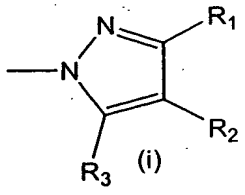


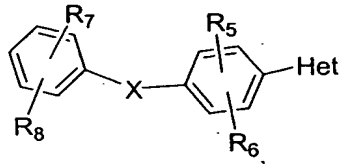
R_1 is $C(O)R_{10}$, $CH_2C(O)R_{10}$, or SO_2R_{10} wherein R_{10} is amino[,] or alkyl, [N-morpholinyl, N-pyrrolidinyl or N-piperazinyl], all of which are optionally substituted;

R_2 and R_3 are independently hydrogen, C_1-C_6 alkyl, C_1-C_6 alkylthio or C_1-C_6 alkylsulfinyl; and

R_5, R_6, R_7 and R_8 are independently selected from the group consisting of hydrogen, halo, halo(C_1-C_6)alkyl, C_1-C_6 alkyl, hydroxy(C_1-C_6)alkyl, amino(C_1-C_6)alkyl, carboxy(C_1-C_6)alkyl, alkoxy(C_1-C_6)alkyl, nitro, amino, C_1-C_6 acylamino, amide, hydroxy, thiol, C_1-C_6 acyloxy, C_1-C_6 alkoxy, carboxy, carbonylamido and C_1-C_6 alkylthiol.

17. (Once Amended) A pharmaceutical composition, comprising the compound of any one of claims [claim] 1, [or] 16, 22, or 25 and a pharmaceutically acceptable carrier.

22. (Three Times Amended) A compound of Formula *I*:



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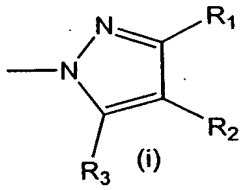
or a pharmaceutically acceptable salt, prodrug or solvate thereof, wherein

X is O or S;

Het is



R_1 is $C(O)R_{10}$, wherein R_{10} is amino[, N-morpholinyl, N-pyrrolidinyl or N-piperazinyl, all of which are optionally substituted];

R_2 and R_3 are independently hydrogen, C_1-C_6 alkyl, C_1-C_6 alkylthio or C_1-C_6 alkylsulfinyl; and

R_5, R_6, R_7 and R_8 are independently selected from the group consisting of hydrogen, halo, halo(C_1-C_6)alkyl, C_1-C_6 alkyl, hydroxy(C_1-C_6)alkyl, amino(C_1-C_6)alkyl, carboxy(C_1-C_6)alkyl, alkoxy(C_1-C_6)alkyl, nitro, amino, C_1-C_6 acylamino, amide, hydroxy, thiol, C_1-C_6 acyloxy, C_1-C_6 alkoxy, carboxy, carbonylamido and C_1-C_6 alkylthiol.

		Due Date:	**None**
Applicants:	Hogenkamp *et al.*	**Art Unit:**	1626
		Examiner:	Shameem, G.
Application No.:	09/814,123	**Docket:**	1861.1270001
Filed:	March 22, 2001	**Atty:**	JMC/THN
For:	**Aryl Substituted Pyrazoles, Triazoles and Tetrazoles, and the Use Thereof**		

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1. SKGF Cover Letter;
2. Supplemental Amendment and Reply; and
3. One (1) return postcard.

		Due Date:	**None**
Applicants:	Hogenkamp *et al.*	**Art Unit:**	1626
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Via Hand Carry
Group Art Unit 1626
Examiner G. Shameem

February 14, 2003

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